REMARKS

I. Introduction

The present application is directed to particulate vaccine compositions. These compositions are particularly useful for mucosal administration of vaccines especially by intra-nasal routes.

Claims 1, 7-8, 10, and 13 have been amended to clarify the features of the invention. Claims 2, 3, 5, 11 and 14-25 have been cancelled without prejudice. Claims 14-26 were directed to a non-elected invention. Claims 26-28 and 30-32 have been withdrawn from consideration as being drawn to a non-elected species. Claim 33 has been newly added. Upon entry of the present amendment, Claims 1, 4, 6-10, and 26-33 will be pending in this application. No new matter is added and support for the amendments is found throughout the specification and in the original claims.

II. Rejections based on 35 U.S.C. § 102

The Examiner has rejected Claims 1, 3-4, 6-9, 12-13 and 29 under 35 U.S.C. § 102(b) as being anticipated by Duncan *et al.* (WO 94/20070). Applicants respectfully traverse this rejection and request reconsideration and withdrawal thereof.

An object of the present application is to enhance the immune response to vaccines, particularly those administered to mucosal surfaces, more specifically the gastrointestinal mucosae. The present application teaches a vaccine composition containing particles of a biologically active agent, as either liposomes or microcapsules, and an adjuvant. In contrast, Duncan *et al.* teach a **four-part** vaccine composed of an immunogen, a mucoadhesive, an adjuvant, and a pharmaceutically suitable delivery vehicle. The compositions of the present application and the Duncan *et al.* composition further differ over the acceptable classes of adjuvants used and how they are incorporated into the composition.

Claim 1 has been amended to clarify that the particles are polymeric microcapsules, they are either obtainable using a double emulsion solvent evaporation method or have an adjuvant chemical incorporated at the surface. Claim 3 has been cancelled without prejudice.

Applicants respectfully submit that Duncan *et al.* fails to disclose "positively charged cationic block copolymers or positively charged cationic surfactants" as immunostimulants as claimed in Claim 1. The Examiner has relied on the teaching of Duncan *et al.* on page 10, line 5, where the term "polycations" is used. This term relates to an enormous class of divergent compounds, and it would be unreasonable to suggest that Duncan *et al.* teach that **all** polycations are immunostimulants. There is no reason why a skilled person in the art would alight on the particular form of polycation, which is the subject of the present application, based on the Duncan *et al.* disclosure. This is particularly true because the possible recited examples, DEAE-4 dextran and polyornithine, are not even closely related examples of block copolymers.

Block copolymers are composed of long sequences ("blocks") of the same monomer unit, covalently bound to sequences of unlike type. The properties of this class of compounds are uniquely important to the proposed composition. Duncan *et al.* disclose a loose association between adjuvant and antigen by stating, "The immunogenic composition of the invention can be prepared by simply mixing the immunogen, mucoadhesive and adjuvant together without covalent bonding or otherwise coupling the ingredients together." (page 14 paragraph 2), with or without the additional option of microencapsulating them. In the present application, the class of adjuvant chemicals were chosen for their known ability or potential to be incorporated within, at the surface, or preferably throughout the microcapsule (page 13, lines 33-35 and page 9, line 13 to page 10, line 6; see also page 14, lines 1-13). Duncan *et al.* fail to disclose or teach the use of adjuvants having the dual function of being an immunostimulant and a functional component of the microcapsule wall.

For at least the above reasons, applicants respectfully submit that the subject matter of Claims 1, 4, 6-9, 12-13 and 29 are novel over Duncan *et al.*

The Examiner has rejected Claims 1, 4, 6-9, 12 and 29 under 35 U.S.C. § 102(a) as being anticipated by Griffin *et al.* (*Vaccine* 16(5):517-521). Applicants respectfully traverse this rejection and request reconsideration and withdrawal thereof.

Griffin *et al* discloses the microencapsulation of V antigen with poly(L)lactide. Applicants strongly maintain that poly(L)lactide is not encompassed in the classes of adjuvants specified in Claim 1. The structure of poly(L)lactide is shown on page 2 of the attached web extract relating to Bioabsorbable Polymers (attached as Exhibit A). Poly(L)lactide clearly contains no amino groups and is not "highly positively charged". Furthermore, poly(L)lactide is not a copolymer. A copolymer must contain more than one type of monomer, and poly(L)lactide is made up of only a single monomer, L-lactic acid. A block copolymer must contain at least two different monomers, which must be arranged in a particular way, specifically in blocks as illustrated in the attached explanation of block copolymers available from the www.princeton.edu website (attached as Exhibit B). For at least the above reasons, applicants respectfully submit that the subject matter of Claims 1, 4, 6, 12-13 and 29 are novel over Griffin *et al.* Claim 3 has been cancelled without prejudice.

The Examiner has rejected Claims 1, 3-4, 6-10, 12-13 and 29 under 35 U.S.C. § 102(e) as being anticipated by Park *et al.* (US 6,267,987). Applicants respectfully traverse this rejection and request reconsideration and withdrawal thereof.

Park *et al.* teach the use of a single copolymer to create a suitable delivery vehicle for biological agents. This single copolymer is the only polymeric component in the composition (Park *et al.*, columns 13-15, Claims 10, 15, 19, and 23). This is entirely different from the compositions disclosed in the present application. "Suitably, the adjuvant chemical which increases the biological effect of the composition in this case is a polymeric material which is different to the polymeric material, where present, of item (iii), above" (page 8 paragraph 2). In contrast to the composition of Park *et al.*, the adjuvant cannot be the sole component of the microcapsule or liposome in the claimed composition.

For at least the above reasons, applicants respectfully submit the subject matter of Claims 1, 4, 6, 12-13 and 29 are novel over Park *et al.*, and Claim 3 has been cancelled without prejudice.

III. Rejections based on 35 U.S.C. § 112, first paragraph

The Examiner has rejected Claims 1, 3-4, 6-10, 12-13 and 29 under U.S.C. § 112, second paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse this rejection and request reconsideration and withdrawal thereof.

The Examiner states, "the instant specification fails to provide any experiments that show that such vaccines would be effective in protecting an animal against any type of infection." The present specification is not drawn to a new generic vaccine claiming to provide wholesale immunity to all diseases in all animals. It is drawn to a composition that, when utilized with known vaccines of known effect and administered non-parenterally, would "facilitate induction of comparable levels of systemic immunity to that elicited by conventional sub-cutaneous and intra-muscular injections" (page 1 lines 14-17). The present specification clearly sets out the nature, including structural details, of the immunostimulants as well as the types of compositions into which they may be incorporated. The nature of the vaccine component would be apparent to the skilled person seeking to make a vaccine against a particular pathogen. The efficacy of the immunostimulants and their abilities to be incorporated into microcapsules has been demonstrated by the experimental data in the Examples and the Figures of the present application. It is therefore clear from these disclosures that the present inventors had possession of the claimed invention.

For at least the foregoing, applicants respectfully submit that they have overcome the Examiner's rejection and request withdrawal thereof.

The Examiner has rejected Claims 1, 3-4, 6-10, 12-13, and 29 under U.S.C. § 112, second paragraph, as failing to comply with the written description requirement. Applicants respectfully submit that no new matter has been added and that the specification as filed

contains support for the composition described in the claims and request withdrawal and reconsideration of the rejections thereof.

Pages 4 and 5, lines 8-12, as well as page 7, lines 14-26, provide support for a vaccine composition comprising pharmaceutically acceptable particles selected from polymeric microcapsules or liposomes wherein the particles comprise a biologically active agent that generates a protective immune response in an animal to which it is administered; in combination with an adjuvant chemical which increases the effect of the biologically active agent by acting as an immunostimulant. Page 6, lines 4-9, provide support for the use of positively charged block copolymers or positively charged surfactants. Page 7, lines 9-12, and pages 13-14, lines 28-13, provide support for the use of microcapsules and liposomes. Claim 1 has been amended to remove the phrase, "when the adjuvant chemical is selected from C, the composition does not contain a polyacrylic acid."

For at least the foregoing, applicants respectfully submit that they have overcome the Examiner's rejection and request withdrawal thereof.

IV. Rejections based on 35 U.S.C. § 112, second paragraph

The Examiner has rejected Claims 1, 3-4, 6-10, 12-13 and 29 under U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully submit that amendments to the claims overcome the rejections and request withdrawal and reconsideration thereof.

Claim 1 was amended to insert the Markush group form of alternate expression.

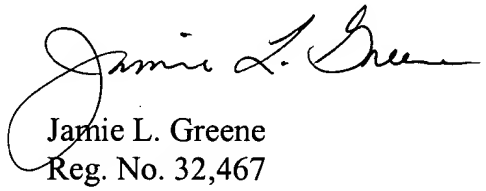
Claims 8 and 10 were amended to recite "microcapsules" to make terminology used throughout the claims consistent.

CONCLUSIONS

In light of the amendments and the above remarks, Applicants are of the opinion that the Office Action has been completely responded to and that the application is now in condition for allowance. Such action is respectfully requested.

If the Examiner believes any informalities remain in the application that may be corrected by Examiner's Amendment, or there are any other issues that can be resolved by telephone interview, a telephone call to the undersigned attorney at (404) 815-6409 is respectfully solicited.

Respectfully submitted,



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